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Vitamin D Intoxication

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HYPERCALCEMIA associated with renal insufficiency has been reported in numerous conditions such as vitamin D intoxication,[1,6] hyperparathyroidism,[3] acute osteoporosis,[2] sarcoidosis,[3,9,10] carcinomatosis with bone involvement,[3,12] multiple myeloma[3,11] and the "milk-alkali syndrome."[4] In 1942, two of the earliest cases in the literature of vitamin D poisoning in adults were described by Tumulty and Howard.[13] Since that time many reports have appeared and the clinical picture has been well described, particularly by Howard and Meyer[8] in 1948, and Chaplin and others in 1951.[7] Despite its toxicity, vitamin D still is sometimes used with little or no justification in conditions such as sarcoidosis, asthma, psoriasis and rheumatoid arthritis, and often results in poisoning. In addition, the general availability of highly concentrated preparations of vitamin D[7] has led to intoxication from self medication. Vitamin D intoxication has also been reported when the substance was being used for specific deficiency states such as osteomalacia secondary to steatorrhea and hypoparathyroidism after thyroidectomy.[5]

In the following case vitamin D intoxication occurred in a case in which a highly concentrated vitamin D product, Darthronol,®* was administered in the treatment of a musculoskeletal condition resembling early rheumatoid arthritis.

From the Santa Cruz Medical Center, Santa Cruz.
Submitted August 15, 1961.

*Darthronol; J. B. Roerig Co., Division Chas. Pfizer, Inc., N. Y.

REPORT OF A CASE

An insurance broker, age 33, otherwise in excellent health, consulted a physician November 6, 1958, because of pain in the forearms, wrists and hands. Darthronol® was prescribed, one tablet (50,000 units) the first day, two tablets the second, and then three daily. After a week of this therapy, the author examined the patient in consultation, and at that time he was complaining of general malaise, headaches, vertigo and pronounced polyuria and polydypsia. Upon physical examination in the office no abnormalities were noted. The urine had specific gravity of 1.009, an acid reaction and a negative reaction for albumin and sugar. On microscopic examination an occasional erythrocyte, 2 to 5 leukocytes and a moderate number of granular casts per high power field were noted. The Sulkowitch reaction was four plus. Vitamin D intoxication was suspected and the patient was advised to stop taking Darthronol®, to ingest no dairy products and to drink 2,500 to 3,000 cc. of plain liquids every 24 hours. He was again seen in his home two days later and the symptoms of headache and vertigo with nausea and vomiting persisted. Serum calcium at that time was 14.1 mg. and inorganic phosphorus content was 1.2 mg. per 100 cc. Because of the persistence of symptoms, the patient was admitted to the hospital for further observation and treatment.

On admission he was nauseated, but not in acute distress. The oral temperature was 98° F., the pulse rate 80 with regular sinus rhythm, respirations 20 per minute and blood pressure 140/90 mm. of mercury. Deep tendon reflexes were hypoactive to absent. The plantar response was flexor. Otherwise

the results of physical examination were within normal limits.

The hematocrit was 48. Leukocytes numbered 10,800 per cu. mm. with 5 per cent eosinophils. The urine, which was clear, had a pH of 7.2, a trace reaction for albumin, a Sulkowitch reaction of two plus and 3 to 5 leukocytes per high power field. Blood urea nitrogen was 115 mg. per 100 cc.; creatinine, 8 mg. per 100 cc.; carbon dioxide combining power 28.4 mEq per liter; chlorides, 105 mEq per liter; calcium, 13.5 mg. per 100 cc.; phosphorus, 3.8 mg. per 100 cc.; phosphatase, 1.3 Bodansky units. Phenolsulfonphthalein excretion was 10 per cent at 15 minutes, 17.5 per cent at 30 minutes, 22.5 per cent at 60 minutes and 37.5 per cent at 120 minutes. Three lupus erythematosus test preparations were negative for LE cells. Results of a rheumotoid slide test were negative. Creatinine clearance was 45 cc. per minute. Serum sodium was 136 mEq per liter; potassium, 4.6 mEq per liter; total protein, 7.7 gm. per 100 cc.—4.5 gm. of albumin and 3.2 gm. of globulin.

A diet containing 125 mg. of calcium and about 4,000 cc. of fluids was provided and within three days blood urea nitrogen was 82 mg., creatinine 3 mg., calcium 12.9 mg. and phosphorus 2.9 mg. per 100 cc. Urinary calcium excretion in 24 hours varied from 450 mg. to more than 600 mg. All dairy foods were excluded from the diet, and cortisone, 10 mg. daily was given for two days, then prednisone in dosage of 30 mg. daily, which was reduced to 10 mg. daily over the last four days in hospital. On the day of discharge, ten days after admission, creatinine clearance was 73 cc. per minute; blood urea nitrogen content was 45 mg., creatinine 1.7 mg., calcium 10.7 mg., phosphorus 2.8 mg. and uric acid 5.1 mg. per 100 cc. Calcium excretion in 24 hours was 84 mg. At the time of discharge, the patient was asymptomatic.

However, although the diagnosis at the time seemed reasonably clear, it was felt that hyperparathyroidism could not be completely excluded, and the patient was kept under observation for some 18 months after the initial episode of illness. Three months after the onset of the previously described symptoms, the urine was normal and the blood urea nitrogen was 14.9 mg. per 100 cc. Twenty-seven months after the onset of illness, the urine continued to remain normal, the Sulkowitch reaction was well within normal limits and the blood urea nitrogen was 12 mg., serum calcium 10.6 mg. and phosphorus 4.0 mg. per 100 cc. Total protein content was 6.6 gm. per 100 cc.—3.6 gm. albumin and 3.0 globulin.

DISCUSSION

The clinical manifestation of vitamin D poisoning is owing to hypercalcemia, *per se*, and to renal failure. The former causes fatigue, depression and loss of weight, and renal failure causes polyuria, with a low specific gravity of urine and a rise in the blood urea nitrogen. Although a normocytic, normochromic anemia may appear in association with the uremia, this did not occur in this case. Vitamin D poisoning may also result in metastatic calcification, affecting not only the kidneys but other organs as well—such as the eye, where ocular deposits and keratitic bands may form. An intravenous pyelogram and x-ray films of the bones showed no evidence of demineralization in this case. Albright and Reifenstein[3] expressed belief that poisoning is due primarily to vitamin D promoting absorption of calcium from the bowel, with hypercalcemia a consequence, then depression of the parathyroid glands, a decrease in urinary phosphorus excretion, and so hyperphosphatemia.

SUMMARY

In a case of vitamin D poisoning herein described, the initial diagnosis for which the patient was being treated with this substance was in doubt. Prompt discontinuance of the drug resulted in the patient's early and complete recovery.

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